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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,818	08/20/2003	Bryan Julien	020547-002110US	8035
7590 02/09/2006			EXAMINER	
Ted Apple Townsend and Townsend and Crew 379 Lytton Avenue Palo Alto, CA 94301			BURKHART, MICHAEL D	
			ART UNIT	PAPER NUMBER
			1633	
DATE MAILED: 02/09/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/645,818

Applicant(s)

JULIEN, BRYAN

Examiner

Michael D. Burkhart

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/21/05.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 1-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 8/20/2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/1/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 16-18 in the reply filed on 12/21/2005 is acknowledged.

Claims 1-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Election was made **without** traverse in the reply filed on 12/21/2005.

Specification

The disclosure is objected to because of the following informalities: the U.S. application number should be filled in on page 8, ¶ [0027].

Appropriate correction is required.

Claim Objections

Claim 16 objected to because of the following informalities: in part a), "a protein with Mx9 integrase activity protein operably linked" should be "a protein with Mx9 integrase activity operably linked". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: providing for the production of epothilone A, B, C, and D, in the host cell. Production of such epothilones occurs only in the bacterium *Sorangium cellulosum*, thus any other host cell would have to be modified to produce the epothilones.

Claim 18 recites the limitation "exogenous gene" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a bacterial host cell produced by a method comprising introducing a Mx9 transformation system into the cell, wherein the system comprises "a gene encoding a protein with Mx9 integrase activity." Applicants disclose the Mx9 integrase gene and that it functions in the claimed transformation system. The claims read on a very large genus of potential proteins with Mx9 integrase activity. The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual

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reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention.

In the instant case, applicants only disclose the Mx9 integrase protein of SEQ ID NO: 2 as functioning in the claimed transformation system by catalyzing the recombination between the *attP* and *attB* sites.. Neither applicants nor the prior art disclose other proteins or mutants with this Mx9 integrase activity. Furthermore, applicants state (page 4, ¶ [0017] to page 5, ¶ [0018]) that the claimed protein with Mx9 integrase activity need only to have 70% sequence identity to the disclosed Mx9 integrase (SEQ ID NO: 2). Applicants provide no basis for deriving other proteins from the Mx9 integrase, such as functional mutants or functional domains of the integrase. Therefore, there is no structural/functional basis provided to envision other embodiments other than the disclosed Mx9 integrase represented by SEQ ID NO; 2. Applicants claim proteins "with Mx9 integrase activity" by function only, without a correlation between structure and function. The prior art does not compensate for the lack of description of specific examples of other proteins with Mx9 integrase activity as claimed. The lack of disclosure and broad genus regarding the claimed proteins "with Mx9 integrase activity" would require the skilled artisan to conclude that the example presented by the applicants are not sufficient to describe the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 16 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Martin et al (Virology, 1978). The claims are product by process claims and thus are not limited *per se* by the process steps, only by the properties of the product produced by the steps. It is considered that a *Myxococcus xanthus* cell infected with the Mx9 bacteriophage comprises all the properties of the claimed bacterial host cell for reasons set forth above in the U.S.C. §101 rejection. Martin et al teach the isolation, from soil, of *M. xanthus* cultures that harbor bacteriophages (see abstract and page 45, first column, first full ¶ to second column, second full ¶) . One such bacteriophage was Mx9, isolated from host strain DK816 (see Table 1). Mx9 comprises exogenous genes relative to *M. xanthus*. The strain DK816 was used in the instant specification to prepare Mx9 bacteriophage, to delineate the *attP* core site (SEQ ID NO: 5) and *attB* sites, and thus inherently comprises SEQ ID NO: 5.

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Claims 16, 17, and 19-21 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Julien et al (U.S. Patent 6,303,342, 2001, cited in the IDS).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are product by process claims and thus are not limited *per se* by the process steps, only by the properties of the product produced by the steps. It is considered that a *Myxococcus xanthus* cell infected with the Mx9 bacteriophage comprises all the properties of the claimed bacterial host cell for reasons set forth above in the U.S.C. §101 and 102(b) rejections. Julien et al teach *M. xanthus* cells producing epothilone C and/or D (claims 1-4). The *M. xanthus* has the chromosomal *attB* site for reasons set forth in the above 101 and 102 (b) rejections. The claimed *M. xanthus* cells can be prepared using phage-based expression vectors that integrate into the *M. xanthus* chromosomal DNA, thus mimicking an integration by Mx9. Phage Mx9 and Mx8 are preferred for these purposes. The integration and attachment function of these phages (e.g. the *attP* site and the Mx9 integrase) can be placed on plasmids to create phage-based expression vectors. See column 37, line 1-13.

Claims 16-21 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Julien et al (U.S. Patent 6,410,301, 2002).

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The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are product by process claims and thus are not limited *per se* by the process steps, only by the properties of the product produced by the steps. It is considered that a *Myxococcus xanthus* cell infected with the Mx9 bacteriophage comprises all the properties of the claimed bacterial host cell for reasons set forth above in the U.S.C. §101 and 102(b) rejections. Julien et al teach *M. xanthus* cells producing epothilone C and/or D (claims 1-6). The *M. xanthus* has the chromosomal *attB* site for reasons set forth in the above 101 and 102(b) rejections. The claimed *M. xanthus* cells can be prepared using phage-based expression vectors that integrate into the *M. xanthus* chromosomal DNA, thus mimicking an integration by Mx9. Phage Mx9 and Mx8 are preferred for these purposes. The integration and attachment function of these phages (e.g. the *attP* site and the Mx9 integrase) can be placed on a transposon. See Example 2, column 35, line 65 to column 36, line 16. The *matB* or *C* genes may also be introduced into the cells (see Example 5, column 38).

Conclusion

No claims are allowed.

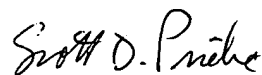
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1633



SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER